UNITED STATES DISTRICT COURT
DISTRICT OF NEW HAMPSHIRE

LISA D. CARPENTER and JEFFREY D. CARPENTER, Plaintiff, vs. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Civil Action No. 1:14-CV-00540-PB Hon. Paul J. Barbadoro **FIRST AMENDED COMPLAINT**

INTRODUCTION

1. Cymbalta (generically known as duloxetine) is a prescription antidepressant manufactured, marketed and sold by Defendant Eli Lilly and Company ("Lilly"). This civil action alleges personal injuries and damages Plaintiffs suffered as a result of Lilly's failure to provide adequate instructions for stopping Cymbalta and an adequate warning that fully and accurately informed Plaintiff about the frequency, severity, and/or duration of symptoms associated with Cymbalta withdrawal in its marketing and labeling. In addition, Plaintiffs allege that Lilly defectively designed Cymbalta pills as delayed-release capsules with beads available only in 20, 30 and 60 mg doses, with a label that instructs users that the drug "should be swallowed whole and should not be chewed or crushed, nor the capsule be opened and its contents be sprinkled on food or mixed with liquids." Lilly's design (delayed-release capsules with beads available only in 20, 30 and 60 mg doses) and accompanying instructions (Cymbalta should be "gradually tapered," but should only be "swallowed whole") prevented Plaintiff from properly tapering off of the drug. Moreover, Lilly never sought to warn patients about this serious design defect in its marketing and labeling.

PARTIES

2. Plaintiffs Lisa D. Carpenter and Jeffrey D. Carpenter are, and at all times relevant to this Complaint were, citizens of the State of New Hampshire and residents of Strafford County. Neither Plaintiff is a resident or citizen of the State of Indiana.

3. Defendant Eli Lilly and Company is, and at all times relevant to this Complaint was, an Indiana corporation with its headquarters and principle place of business in Indianapolis, Indiana. Lilly is a pharmaceutical company involved in the research, development, testing, manufacture, production, promotion, distribution, marketing, and sale of numerous pharmaceutical products, including Cymbalta.

JURISDICTION AND VENUE

4. This Court has subject matter jurisdiction pursuant to 28 U.S.C.A. § 1332. There is complete diversity of citizenship between Plaintiffs and Lilly and the amount in controversy exceeds $75,000.00, exclusive of interest and costs.

5. This Court has personal jurisdiction over Lilly because Lilly has purposefully directed its marketing and sales of numerous pharmaceutical products to the State of New Hampshire. Lilly has had substantial contacts with the State of New Hampshire such that maintenance of the action is consistent with traditional notions of fair play and substantial justice.

6. Furthermore, Lilly has caused tortious injury by acts and omissions in the State of New Hampshire, as well as caused tortious injury by acts and omissions outside of the State of New Hampshire, while regularly doing and soliciting business, engaging in a persistent course of conduct, and deriving substantial revenue from goods used or consumed and services rendered in the State of New Hampshire.

7. Venue is proper before this Court pursuant to 28 U.S.C. § 1391. A substantial portion of the events giving rise to the claims alleged in this Complaint took place within the District of New Hampshire.

FACTUAL ALLEGATIONS

8. Lilly is one of the largest pharmaceutical companies in the world with annual revenues exceeding $20 billion. A substantial portion of Lilly's sales and profits have been derived from Cymbalta, whose 2013 annual sales exceeded $3.9 billion. Worldwide, Cymbalta is one of the few prescription drugs whose sale eclipsed $5 billion in a single year.

9. Lilly has enjoyed considerable financial success from manufacturing and selling antidepressants, including Prozac (generically known as fluoxetine). Lilly launched Prozac in 1988, touting it as the first "Selective Serotonin Reuptake Inhibitor" ("SSRI"). SSRIs are a class of antidepressant drugs that have been promoted as increasing the brain chemical serotonin in the synaptic clefts between the neurons in the brain. Prozac became extremely popular in the 1990s and was the top selling antidepressant of its kind. Prozac's patent expired in August 2001, leading to a proliferation of generic versions of the drug.

10. In 2001, Lilly needed to fill the void left behind by Prozac's patent expiration, and so it sought approval by the Food and Drug Administration ("FDA") for its next patented antidepressant, Cymbalta. Cymbalta belongs to a class of antidepressants known as "Serotonin and Norepinephrine Reuptake Inhibitors" ("SNRIs"). SNRIs are similar to SSRIs, but in addition to blocking the absorption of serotonin, SNRIs are thought to block the absorption of another neurotransmitter, norepinephrine, thereby increasing the levels of both serotonin and norepinephrine in the brain. These drugs are promoted as treatments for pain as well as depression.

11. The FDA initially rejected Lilly's application in 2003 for approval of Cymbalta due to certain violations of good manufacturing practices and the risk of liver toxicity apparent in the drug's safety profile.

12. Eventually, in 2004, the FDA approved Cymbalta with a liver toxicity warning included in the prescribing information. The drug was approved for Major Depressive Disorder ("MDD"). In 2007, the FDA approved Cymbalta for treatment of Generalized Anxiety Disorder ("GAD") and in 2008 for treatment of fibromyalgia.

13. Since the FDA's initial approval of Cymbalta in 2004, Lilly has aggressively marketed the drug to the public and the medical community, spending millions of dollars each year on advertising and promotion. Lilly has promoted Cymbalta directly to consumers, including Plaintiff Lisa D. Carpenter, through various media platforms, including internet, print and television. In addition, Lilly has promoted Cymbalta to the medical community by utilizing its well-organized army of sales representatives to personally visit physicians and health care professionals to distribute free drug samples and promotional literature.

14. Lilly's promotional campaigns have continuously failed to provide adequate instructions to users and health care professionals for stopping Cymbalta and have failed to include adequate warnings that fully and accurately inform users and health care professionals about the frequency, severity, and/or duration of Cymbalta withdrawal. This failure to warn and disclose information is not limited to the Cymbalta labeling, but contemplates all of Lilly's marketing efforts, i.e., direct-to-consumer marketing, direct-to-prescriber marketing, sales representatives, "dear doctor" letters, and the Cymbalta labeling.

15. Withdrawal symptoms are not connected to a patient's underlying condition but rather are the body's physical reactions to the drug leaving the system and, after the drugs have left, repairing the damage caused to the patient's nervous system by the long-term use of the

drug. While many SSRIs and SNRIs can cause withdrawal symptoms, the initiation, frequency, and severity of withdrawal symptoms generally correlate to a drug's half-life. The half-life of a drug is the time it takes for the concentration of the drug in the body to be reduced by half. This information is one of the basic pharmacokinetic properties of a drug and is known to researchers developing the drug. Cymbalta has one of the shortest half-lives of any of the SSRIs and SNRIs. Since 2004, the Cymbalta label has stated that the half-life of Cymbalta is approximately 12 hours. In contrast, the half-life of Prozac is seven days. The shorter the half-life, the faster the body eliminates the drug from the system, thus creating a higher risk of withdrawal symptoms. Because Cymbalta's half-life is less than one day and Cymbalta is generally administered once daily, it is possible for users of Cymbalta to experience withdrawal symptoms after simply forgetting to take one dose. This also means that users cannot safely taper off of the drug by taking a capsule every other day.

16. Despite Lilly's awareness of Cymbalta's half-life and the correlation between a short half-life and withdrawal risk, Lilly did not include any cross-references between the Pharmacokinetics section of the label and either the Precautions section or the Dosage and Use section. In fact, rather than drawing attention to the potential consequences of Cymbalta's extremely short half-life, Lilly misleadingly referenced all other SSRIs and SNRIs, as if Cymbalta could be expected to pose a similar risk of withdrawal as all other drugs of its class generally:

> During marketing of other SSRIs and SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g. paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional liability, insomnia, hypomania, tinnitus, and seizures. Although these events are generally self-limiting, some have been reported to be severe.

(2004 Cymbalta label.) The extremely short half-life of Cymbalta should have alerted Lilly's researchers to the fact that the risk of Cymbalta withdrawal would be more frequent than that experienced with other SSRIs and SNRIs. This information created a duty to systematically investigate this issue as part of Lilly's clinical trial programs.

17. Lilly should have been aware of the significance of antidepressant withdrawal, because Lilly had previously researched and publicized the issue in connection with its antidepressant Prozac. Because Prozac has an extremely long half-life relative to other antidepressants, the length of time it takes for a person's body to fully eliminate Prozac from the system provides a built-in gradual tapering of sorts, so that withdrawal symptoms from Prozac are relatively infrequent. Prozac's main competitors in the 1990s, Zoloft and Paxil, had shorter half-lives, and Lilly engineered a marketing and research campaign to differentiate Prozac from its competitors on this basis, funding clinical studies of antidepressant withdrawal and coining the term "antidepressant discontinuation syndrome."

18. In a marketing report conducted in 2000, Lilly's marketing research recommended that Lilly "[c]onsider expanding on the idea that Prozac's long half-life prevents discontinuation syndrome, making direct comparisons to Paxil and Zoloft."

19. In an email dated November 11, 2002, a Lilly physician Walter Deberdt was giving comments about an expert report related to Cymbalta, and in the email he acknowledged Lilly's role in cultivating the withdrawal issue in its marketing of Prozac. In the email, he commented: "Discontinuation symptoms are a big deal in MDD [Major Depressive Disorder] (thanks to ourselves with Prozac promotion)."

20. Researchers, including Lilly's own consultants, have postulated that withdrawal reactions result from a sudden decrease in the availability of synaptic serotonin in the face of down-regulated serotonin receptors. *See* Schatzberg et al., Possible mechanisms of the serotonin

reuptake inhibitor discontinuation syndrome, J. Clin Psychiatry 58 (suppl7): 23-7 (1997); Blier and Tremblay, Physiological mechanisms underlying the anti-depressant discontinuation syndrome, J Clin Psychiatry 67 (suppl4) (2006): 8-13. They have theorized that, upon chronic dosing, the increased occupancy of pre-synaptic serotonin receptors signals the pre-synaptic neuron to synthesize and release less serotonin. Serotonin levels within the synapse drop, then rise again, ultimately leading to down-regulation of post-synaptic serotonin receptors. In other words, as SSRIs and SNRIs block the reuptake of serotonin and norepinephrine, structural changes in the brain occur such that production of these neurotransmitters is reduced. These changes in the brain's architecture may contribute to withdrawal symptoms, as a patient is, upon cessation of the drug, left not only with the absence of the drug but also structural changes in the brain that remain for some time even after the drug has fully washed out of the person's system. Because of the short half-life of Cymbalta, the brain has even less time to adjust to the cessation of Cymbalta treatment. Despite Lilly's knowledge of this phenomenon, Lilly did not include in Cymbalta's label or promotional materials any information regarding the increased risk of withdrawal due to structural changes in the brain exacerbated by Cymbalta's short half-life.

21. Before Cymbalta was approved by the FDA, Lilly was fully aware of the issue of antidepressant withdrawal and of Cymbalta's elevated withdrawal risk. Lilly should not only have included a strong warning to physicians and patients in its marketing and labeling, but it should have also designed the drug in such a way that would easily allow for a gradual tapering of the drug below 20 mg. Lilly had this duty and obligation prior to seeking FDA approval. Instead, Cymbalta was submitted for FDA approval, and was ultimately approved, as a delayed-release capsule filled with tiny beads at 20, 30 and 60 mg doses only. Moreover, Cymbalta's label and Medication Guide instruct physicians and patients that the capsule "should be swallowed whole and should not be chewed or crushed, nor should the capsule be opened and its

contents be sprinkled on food or mixed with liquids." This instruction exists because alteration of the Cymbalta capsule can alter the capsule's enteric coating making the drug indigestible. This is in contrast to other SSRIs and SNRIs (most of which existed on the market before Cymbalta's approval) that are available as scored tablets that can be halved and quartered with relative ease, or are available in liquid form which can be measured and dispensed in small increments. Before Cymbalta was ever approved, Lilly knew that a 20 mg dose would not adequately reduce the risk of withdrawal but took no action to seek approval of smaller tapering doses to allow patients to safety discontinue Cymbalta below 20 mg.

22. In 2012, Cymbalta's label provided the following precaution regarding stopping Cymbalta:

> Discontinuation symptoms have been systematically evaluated in patients taking duloxetine. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at 1% or greater and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis. . .

Cymbalta's label also provided the following instructions for stopping Cymbalta:

> A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate.

Id.

23. Thus, in addition to using the euphemistic term "discontinuation" to describe Cymbalta's withdrawal symptoms, the label did not accurately reflect that a significant percentage of Cymbalta users suffered from withdrawal symptoms. Rather, the warnings suggested that Cymbalta withdrawal was rare, or occurred at a rate of approximately one (1) percent. However, Lilly's own studies, published in a November 2005 article in the Journal of Affective Disorders, showed that, at a minimum, between 44.3% and 50% of Cymbalta patients

suffered from "discontinuation" side effects (i.e., withdrawal symptoms). The article also noted that the withdrawal symptom data compiled during Lilly's clinical trials was gathered from "spontaneous reports" of symptoms (patients volunteering symptoms), and not using the more accurate "symptom checklist." The authors acknowledge that use of a symptom checklist would likely produce even higher incidence rates of withdrawal symptoms. David G. Perahia et al., Symptoms Following Abrupt Discontinuation of Duloxetine Treatment in Patients with Major Depressive Disorder, 89 JOURNAL OF AFFECTIVE DISORDERS 207 (2005). Although the studies discussed in the published article were submitted to the FDA, the pooled analysis of the studies was not. The analysis and conclusions drawn in the Perahia article were not considered as part of Cymbalta's original FDA approval.

24. Lilly omitted this critical information from its label, instead misleadingly stating only that certain symptoms are experienced at a rate of 1% or greater, thus suggesting that Cymbalta withdrawal is rare or infrequent.

25. Moreover, data from the clinical trials in the Perahia article showed that, overall, between 9.6% and 17.2% of Cymbalta users suffered *severe* withdrawal symptoms, *id.*, yet nowhere in the label does Lilly inform practitioners and patients of that risk.

26. On May 3, 2002, two years before Cymbalta's launch in the U.S., a marketing company Brintnall & Nicolini, Inc., presented a market report to Lilly titled "Duloxetine CELA for Depression U.S. Launch: PSYCHs and PCPs" outlining how psychiatrists and primary care physicians would respond to the launch of Cymbalta (duloxetine) in the U.S. In the presentation, the researchers indicated that physicians' responses to Effexor (an already approved serotonin and norepinephrine reuptake inhibitor (SNRI)) would be a good way to predict how physicians would respond to Cymbalta. One of the physicians' primary concerns centered on the "side effects seen with Effexor during use or ***on discontinuation***[.]" The researchers learned that

some primary care physicians were "uncomfortable with Effexor reserving it for 2nd line due to its side effects on starting and tapering patients" and that some psychiatrists "express[ed] disappointment with Effexor's nausea, withdrawal symptoms and remission rates[.]" The report also pointed out that one of the selling points for physicians and psychiatrists about Cymblata would be the "[w]ithdrawal symptoms in comparison with those of Effexor" suggesting that Cymbalta could be marketed as having a superior withdrawal profile.

27. Two months later, on July 8, 2002, a marketing research firm, Ipsos Reid Healthcare, presented the results of a marketing survey. The survey revealed that one of the main advantages of Cymbalta, as presented to physicians, was Cymbalta's low/no discontinuation reaction, on par with being well tolerated and having QD (once-a-day) dosing. The survey also revealed that one of the physicians' major concerns about Cymbalta was its "discontinuation reaction," on par with concerns about sexual dysfunction and risk of nausea. This study confirmed what the prior study had shown—the risks of withdrawal were an important consideration in physicians' view of Cymbalta.

28. On August 2, 2002, the research firm Roberta, Miller & Associates, presented the results of a U.S. Strategic Pricing Study for Cymbalta. The study explored what attributes influenced third-party payors, physicians, and patients' view of an antidepressant and how that influenced their willingness to pay. One important consideration among third-party payors was that Cymbalta would be compared to Effexor and, based on the profile for Cymbalta presented, third-party payors expected Cymbalta to enter the market at about 20% less than Effexor. The slides reflect an important fact—one of the only "factors" that "could justify or warrant consideration of premium pricing relative to Effexor" was if Cymbalta possessed "a significant decrease in rate and severity of withdrawal / discontinuation syndrome." Indeed, for Lilly to price Cymbalta above other antidepressants, "[m]inimization of withdrawal syndrome is seen as

important." This document shows that Lilly had a specified and articulated motive to promote Cymbalta as having a low risk of withdrawal, and that Lilly knew about this issue over two years before Cymbalta was ever approved by the FDA.

29. In July 2003—several months before Cymbalta was approved—the problem with Cymbalta's withdrawal risk profile was raised among Lilly executives. Dr. David Perahia, the man who later went on to help author the Perahia article, sent an email to Michael J. Detke, the Cymbalta & Prozac Global Medical Director:

> Quick question: I was recently asked whether we have discontinuation data at around 3 days post-discontinuation, this being the time when you might expect maximal symptomatology (approx. 5 half-lives after final dose). I didn't think we did, but thought I'd check.

30. Dr. Detke responded that Lilly does not "have data broken out in finer temporal internals[.]" This prompted a frank response from Dr. Perahia:

> I must confess to being a little unconfortable [sic] about the whole discontinuation thing. Maybe it's more of a UK specific issue, but paroxetine [Paxil] is taking a fearsome battering in the media over here at the moment, and a significant part of that is discontinuation-related stuff. It's clear that duloxetine has a significant DESS [discontinuation-emergent signs and symptoms] liability (on abrupt discontinuation, admittedly, but how much taper data do we have yet ?), and the perception will be further reinforced by our short [half-life] which is seen by many as being directly linked [redacted without explanation].
>
> … If we're not careful, the environment is set for this to blow up in our faces unless we're proactive about it.

31. Lilly scientists were acutely aware that having a withdrawal risk profile similar to Paxil posed "significant DESS liability" and could "blow up in [their] faces[.]" Dr. Detke responded by dismissing the issue because he believed that when Lilly was making a big deal about discontinuation in the U.S. with regard to Prozac, it was not particularly successful. He also solicited the opinion of Dr. Madelaine Wohlreich, a lead research physician for Cymbalta in Lilly's United States Affiliate. She responded:

> The feeling here has been that since it will be in our FDA label that tapering is

recommended, that there is not a lot more that needs to be done proactively.

When we have said at consulting conferences that discontinuation type side effects could be seen on abrupt taper, clinicians have not appeared to be terribly concerned.

32. Dr. Perahia responded:

It's not that the discontinuation issue will necessarily be something we can proactively use to sell duloxetine (I believe not, at least from a historical perspective), more that it's something that the media and regulatory authorities might well latch on to unless we are proactive about it. I sense we are being a bit complacent around this, and it could hurt us (e.g. no diffs from parox on abrupt discontinuation in our trials, short t1/2 etc. etc.)

As an opening gambit, I would define proactive as:

(1) Write up our data and get it published as a priority rather than dragging our heels

(2) Consider running a trial which might add to the evidence base on how best to manage stopping the drug, e.g. over how long should drug be tapered? (open label treatment, then perhaps 3 arms looking at abrupt discontinuation vs. 2 week taper vs. 4 week taper in a double blind fashion, with frequent visits). Good PR due to being open and pushing the science, with an evidence-based recommendation at the end to boot. I'm sure Matt would blanch at this suggestion, but we can't just stick our head into the sand.

Paroxetine is being torn to pieces by the media (and in fact regulators too) over in Europe, and much of the criticism is stemming from the perception that GSK have been, to put it politely, less than transparent about discontinuation with paroxetine and how best to manage it. I would rather we didn't fall into the same trap.

33. Dr. Perahia's proposal to conduct clinical trials to figure out "how best to manage stopping the drug," was never done. Lilly never evaluated "how long should [the] drug be tapered" or developed "evidence-based recommendation[s]."

34. Internal documents show that, in 2003, before Cymbalta was even approved by the FDA, Lilly recognized that withdrawal risk adversely impacted the marketability of an antidepressant. In a document titled, "The Market and Competition for Cymbalta," which was created in March 2003, Lilly marketers identified one of paroxetine's (Paxil) primary marketing

weakness, noting "Discontinuation-emergent side effects are very bothersome." Similarly, for venlafaxine (Effexor), Lilly pointed out that "[i]ts short half-life can lead to discontinuation-emergent side effects." Lilly was aware of the marketing stigma associated with having a short half-life and an unfavorable withdrawal profile.

35. On August 17, 2004, just two weeks after Cymbalta was approved by the U.S. Food and Drug Administration, Boehringer Ingelheim presented a "Patient Segmentation Study" designed to isolate what motivates physicians to prescribe antidepressants. Under the section "Factors Influencing Doctor's Selection of an Antidepressant" it states that the most important factor is "avoid dependence / withdrawal issues." The document explains that "[t]he results show that when promoting Cymbalta to doctors . . . 'Avoid dependence / withdrawal issues' . . . must be addressed in order for a productive communication." Later in the study, the researchers try to unpack the "avoid dependence / withdrawal issues" and explain that it "is one of the important factors in selecting an antidepressant" and thus "can be used as an opportunity for Cymbalta." Following a comprehensive analysis of physician preferences, the researchers conclude that, in marketing Cymbalta to physicians, "avoid dependence / withdrawal issues" is one of the four primary factors influencing physician prescribing practices. And, specifically for general practitioners, "less side effect profile and 'it does not cause dependence' ***have to be stressed***[.]"

36. Plaintiffs allege that, in an effort to avoid obtaining "bad data" about the risks of withdrawal, Lilly deliberately avoided using symptom checklists in evaluating withdrawal reactions. Internal Lilly documents confirm this. In all but two of the clinical trials that Lilly has completed on Cymbalta, both pre-approval and post approval, Lilly did not use a symptom checklist to measure withdrawal symptoms. In May 2008, a Lilly researcher working on a different Lilly product emailed Dr. Detke about using a symptom checklist:

> The iGluR5 team is looking at incorporating a withdrawal symptom checklist into our Phase 2 trials. We're thinking about utilizing the Rickel's symptom checklist, however I was asked to check with the duloxetine and atomoxetine teams to see what scale they may have utilized early in their development. Would either of you know for your respective compound what scale was used to verify that there were no discontinuation symptoms?
>
> Would you have any clue, Mike, what was initially used in the early phase duloxetine trials? I looked in our retrospective database and didn't see anything come up as a withdrawal scale.

In response, Dr. Detke stated that "We didn't use any elicited scales. The data that exist are nicely summarized in a Perahia paper." Dr. Detke then explained "[i]f you use an elicited scale, you'll see higher rates. This WILL end up in the label." Dr. Detke knew that use of a symptom checklist would lead to higher incident rates and he expressed concern that such information would end up being in the label. Thus, it appears that Lilly chose to not systematically study Cymbalta withdrawal with the checklist that Lilly, itself, developed for Prozac.

37. It turns out, however, that Lilly did measure withdrawal reactions using a symptom checklist in two studies comparing Cymbalta against Effexor. Lilly decided to use a taper period (Study Period IV) to measure discontinuation symptoms and wanted data showing a difference between Cymbalta and Effexor. According to Dr. Perahia, in an email from 2002:

> I see a number of reasons for having a study period IV, most importantly . . . Individuals both inside and outside Lilly have suggested that DESS might provide a significant area of difference between the drugs favouring Cymbalta, so an appropriately-designed taper period may yield valuable data.

The studies, HMBU & HMCQ, which were completed *after* Cymbalta was approved by the FDA, had a two-week taper period, wherein patients were stepped off of Cymbalta 30 mg each week. During the taper period, patients were assessed for withdrawal reactions using the Association for Methodology and Documentation in Psychiatry scale. For Study HMBU, the results showed that, using the AMDP-5 checklist, 78.1% of patients who tapered off Cymbalta experienced at least one withdrawal reaction. For Study HMCQ, using the AMDP-5 checklist,

74.1% of patients who tapered off Cymbalta experienced at least one withdrawal reaction. The results of Studies HMBU and HMCQ were never shared or considered by the FDA prior to Cymbalta's approval in 2004.

38. Thus, in the two studies where Lilly used a symptom checklist to measure withdrawal reactions for patients tapering off Cymbalta, the data showed that approximately 74%-78% of patients experienced withdrawal. This is almost double the rate observed in the Perahia article, i.e., 44.3%, where only abrupt symptoms were measured without a symptom checklist. This data was never included in the Cymbalta label and was never published in any medical journal—even though Lilly did publish similar data about Prozac in 1998.

39. After Cymbalta was approved by the FDA, Lilly conducted a clinical trial wherein Lilly specifically measured whether tapered versus abrupt discontinutaiton affected the likelihood of withdrawal. The study, HMBR, which was completed in March 2006, contained a discontinuation phase, wherein patients were either abruptly discontinued off the drug or tapered over a two week period. The taper period contemplated a 50% dose reduction each week until 30mg. The results of the study showed that, while there was a difference between Cymbalta and placebo in the emergence of withdrawal symptoms, there was no difference between tapering or abruptly discontinuing within the Cymbalta treatment groups.

40. In email correspondence in 2006 between Lilly personnel about the submission of a supplemental application to the FDA, Lilly had originally proposed the following language to the FDA:

> Discontinuation symptoms have been systematically evaluated in patients taking Cymbalta. Following abrupt discontinuation in placebo-controlled clinical trials of up to 10-weeks duration, the following symptoms occurred at a rate greater than or equal to 2% and at a significantly higher rate in either the MDD or GAD Cymbalta-treated patients compared to those discontinuing from placebo: dizziness; nausea; headache; paresthesia; vomiting; irritability; and nightmare. When patients were tapered over 2 weeks after acute treatment in 9 or 10 week

> GAD studies, no adverse events met criteria as described above.

However, several physicians within Lilly felt that the last sentence of this paragraph was misleading and inaccurate. In an email, Dr. Richard Bump, expressed:

> [C]oncern that the implication from the wording is that tapering eliminates the risk of discontinuation symptoms. None of the individual studies specifically designed to look at this (SUI or GAD) have shown a benefit to tapere compare with abrupt discontinuation. I just believe the sentence that concludes the first paragraph is not accurately reflecting the lack of benefit (or lack thereof) of tapering in studies designed to look at this specifically.

In response, Dr. Detke agreed that the last sentence should be removed because:

> Overall, it strongly implies that tapering substantially improves tolerability, which does not represent the data accurately. To Rick's point, it (perhaps more weakly) implies that tapering solves all tolerability problems entirely, which would be an even worse misinterpretation of the actual data.

Dr. Detke explained during a deposition on April 28, 2015, when asked about this email, that "You wouldn't want to reassure prescribers that if you taper there's no chance of discontinuation-emergent adverse events. That would -- that would – it's false information and it would falsely reassure people." In the email, Dr. Detke, went on to also express concern with a sentence in the label (which existed in 2004), that read: "A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible." Dr. Detke explained that the:

> [S]entence still indicates that tapering is recommended, and is inconsistent, but I would not recommend removing it now because 1) it's from previous class labeling and not worth the fight, and more importantly 2) it may still help patients to taper and almost certainly won't hurt them in the vast majority of clinical situations[.]"

Dr. Detke acknowledged that the data did not support any benefit from tapering and that the class labeling is inconsistent on this point, but did not recommend changing the label because it is "not worth the fight" and "it may still help patients to taper[.]"

41. After Study HMBR, Lilly did not conduct further clinical trials wherein abrupt and tapered discontinuations were directly compared. According to Dr. Detke, the observed

differences between tapering and abrupt discontinuation were too small to warrant further investigation.

42. In addition to the three clinical trials identified above, following Cymbalta's approval, Lilly conducted nearly one hundred clinical trials wherein discontinuation symptoms were measured, albeit without any symptom checklist. These studies, for the most part, indicated that the risk of suffering from withdrawal upon abrupt or tapered discontinuation was significantly higher than the "1% or greater" included on the Cymbalta drug label. Lilly, in possession of such information, was able to strengthen the Cymbalta warning label to adequately warn patients and doctors about the frequency, severity, and duration of Cymbalta withdrawal, and provide evidenced-based recommendations about how to safely (if at all possible) to discontinue Cymbalta. Indeed, on July 18, 2014, a representative for Lilly pursuant to Fed. R. Civ. P. 30(b)(6) testified as follows:

> Q. If Lilly wanted to strengthen the warning for Cymbalta discontinuation syndrome, could Lilly do so and distribute that warning before they obtained FDA approval?
>
> A. There is a mechanism called "changes being [e]ffected" label supplement that can be submitted to the agency at the same time that a company implemented a label change. . . .
>
> Q. So a drug company can decide to give a stronger additional warning about their drugs at any time subject to later FDA approval?
>
> A. Yes.

In 2007, the Division of Medication Errors and Technical Support ("DMETS") within the FDA issued a Memorandum related to Cymbalta. The Memorandum "identified a signal involving the opening of Cymbalta capsules prior to administration to achieve a lower dose of the drug" during "routine post-marketing surveillance[.]" The Memorandum also specifically identified cases wherein patients were "opening the capsules to create a dose of Cymbalta less than 20 mg in an attempt to reduce the adverse events associated with the discontinuation of Cymbalta."

This Memorandum, thus, identifies a safety signal about patients breaking open Cymbalta 20 mg capsules to obtain smaller doses, and some of those were because of withdrawal.

43. Lilly was aware of the design problems with Cymbalta before the drug was approved. However, following the safety signal identified by the FDA in 2007, Lilly was again apprised of its serious design flaw and was under an obligation to warn patients about this issue in its marketing, i.e., the submission of a "dear doctor" letter, and labeling. Lilly, however, took no action to comply with its obligations under the law. Indeed, Matthew Kuntz, a regulatory executive within Lilly who received this 2007 FDA memorandum, admitted during a deposition on May 6, 2015, that Lilly could have utilized the Changes Being Effected regulation to make unilateral changes to the Cymbalta labeling about Cymbalta's 20 mg design defect.

44. On October 3, 2012, the Institute for Safe Medication Practices issued a QuarterWatch report, which Lilly received a preliminary copy of prior to publication. The report concluded:

> We investigated a signal for duloxetine (CYMBALTA) and serious withdrawal symptoms. In the first quarter of 2012, 48 case reports of withdrawal described an array of problems that included neurological effects such as paresthesia and dizziness, psychiatric problems such as crying, suicidal ideation, and anger, and other symptoms including effects on appetite and weight gain. Early clinical studies of abrupt discontinuation showed that withdrawal effects occurred in 40 to 50% of patients, that 10% of those were severe, and that approximately half had not resolved when side effects monitoring ended after one or two weeks. Serious withdrawal symptoms are not unique to duloxetine, and occur with several other antidepressants, benzodiazepines, amphetamines, and opioids. However, in the full report we study a single drug, duloxetine, in depth and find major shortcomings in the official information for both patients and health care professionals.

45. Cymbalta's withdrawal symptoms include, among other things, headaches, dizziness, nausea, fatigue, diarrhea, paresthesia, vomiting, irritability, nightmares, insomnia, anxiety, hyperhidrosis, sensory disturbances, electric shock sensations, seizures, suicidality, and vertigo. When users try to stop taking Cymbalta, the side effects can be severe enough to force them to start taking Cymbalta again, not to treat their underlying conditions, but simply to stop

the withdrawal symptoms. Users thus become prisoners to Cymbalta, and Lilly financially benefits by having a legion of physically dependent, long-term users of Cymbalta.

46. And, as set forth above, the design of Cymbalta pills, as delayed-release capsules filled with tiny beads at 20, 30 and 60 mg doses only, along with the instruction to swallow them whole, prevents users from properly tapering (gradually decreasing their dosage) from Cymbalta in order to avoid or reduce withdrawal symptoms. Lilly did not warn about this issue in any of its labeling or marketing efforts.

47. Despite Lilly's knowledge of the high rate of withdrawal symptoms in users stopping Cymbalta, Lilly neither provided adequate instructions to users and physicians for stopping Cymbalta nor included adequate warnings in its product label, marketing, or advertising to fully and accurately inform users and physicians about the frequency, severity, and/or duration of the withdrawal symptoms.

48. Lilly's misleading direct-to-consumer promotional campaigns and its failure to adequately warn users and physicians about the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms have paid off financially for Lilly. Cymbalta became a "blockbuster" drug with over $3.9 billion dollars in annual sales. In the last few years prior before losing patent exclusivity, Cymbalta was either been the most profitable or second most profitable drug in Lilly's product line. Lilly had the knowledge, the means, and the duty to provide adequate instructions for stopping Cymbalta and adequate warnings about the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms.

49. Lilly could have complied with its obligations to warn patients and doctors and relayed instructions and warnings through the same means it utilized to promote its products, which included but are not limited to its labeling, "Dear Doctor letters," advertisements, and sales representatives. For example, shortly after Cymbalta was approved, Lilly created a medical

information letter titled "Discontinuation Symptoms," which was supposed to be sent to physicians who specifically requested additional information about Cymbalta withdrawal. The original letter, which was approved by the FDA in October 2004, did not include the Perahia analysis since it had not yet been completed or published. In 2006, the letter was updated to include detailed information from Lilly's clinical trials and the results of the Dr. David Perahia's analysis as published in David G. Perahia et al., Symptoms Following Abrupt Discontinuation of Duloxetine Treatment in Patients with Major Depressive Disorder, 89 JOURNAL OF AFFECTIVE DISORDERS 207 (2005). This 2006 letter, however, which was approved by the FDA, was never sent to Plaintiff Lisa Carpenter's physician. Nothing prevented Lilly from issuing this letter to all physicians as a part of a "dear doctor" letter. However, because the letter was only used when a physician specifically requested it, Lilly has only sent out, in total, about 1,000 of these letters over the course of 11 years.

50. Falsely reassured by the misleading manner in which Lilly reported Cymbalta's withdrawal symptoms, physicians, including Plaintiff Lisa D. Carpenter's physician, have prescribed, and continue to prescribe, Cymbalta to patients without adequate instructions for stopping Cymbalta and without adequate warnings that fully and accurately inform them about the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms.

51. At all times relevant, Lilly knew or should have known of the significantly increased risk of withdrawal symptoms, including their severity and duration, posed by Cymbalta and yet failed to adequately warn about said risks.

52. At all times relevant, Lilly engaged in willful, wanton, and reckless conduct, including its defective design of Cymbalta and its failure to fully and accurately warn about the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms, all of which induced

physicians to prescribe Cymbalta and consumers to use it, including Plaintiff Lisa D. Carpenter and her physicians.

53. Plaintiff Lisa D. Carpenter's use of the drug and consequent injuries and damages were a direct and proximate result of Lilly's acts and omissions relating to its failure to provide adequate instructions for stopping Cymbalta and its failure to include adequate warnings that fully and accurately inform users and physicians of the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms.

54. In or around June 2011, Plaintiff Lisa D. Carpenter was prescribed Cymbalta by her physician, for treatment Fibromyalgia.

55. In or around January 2012, Plaintiff Lisa D. Carpenter did not feel that Cymbalta was effectively treating her Fibromyalgia. As a result, Plaintiff Lisa D. Carpenter elected to wean off of Cymbalta under the care and supervision of her physician.

56. Plaintiff Lisa D. Carpenter experienced severe and dangerous withdrawal symptoms upon attempting to discontinue Cymbalta. By way of example, Plaintiff Lisa D. Carpenter experienced nausea, twitching, insomnia, Restless Leg Syndrome, throbbing pain in legs and arms, headaches, eye aches, excessive sweating, chills, tiredness and flu-like symptoms.

57. At all times relevant, including the period prior to Cymbata's approval, Lilly knew or should have known that Cymbalta was in a defective condition and was and is inherently dangerous and unsafe when used in the manner instructed and provided for by Lilly.

58. If Lilly had adequately, accurately and properly warned about the withdrawal symptoms associated with stopping Cymbalta, including accurately reporting their frequency, severity, and/or duration, Plaintiff Lisa D. Carpenter's physician either would not have prescribed the drug to Plaintiff Lisa D. Carpenter; Plaintiff Lisa D. Carpenter would have refused the drug; and/or Plaintiff Lisa D. Carpenter's physician would have been able to more

adequately, accurately and properly weigh and convey the risks and benefits of the drug in a way as to avoid Plaintiff Lisa D. Carpenter's injuries and damages.

59. As a direct and proximate result of taking Cymbalta, Plaintiffs suffered compensable injuries, including but not limited to the following:

a. physical, emotional, and psychological injuries;

b. past and future pain and suffering;

c. past and future mental anguish;

d. loss of enjoyment of life;

e. past and future medical and related expenses; and

f. loss of consortium and companionship.

FIRST CAUSE OF ACTION
NEGLIGENCE

60. Plaintiffs incorporate by reference, as if fully set forth herein, all other paragraphs of this First Amended Complaint.

61. Lilly owed to Plaintiff Lisa D. Carpenter, and to other consumers and patients, a duty to exercise reasonable care in the design, formulation, manufacture, sale, promotion, supply and/or distribution of Cymbalta, including the duty to ensure that the product carries adequate instructions and warnings and that the product does not cause users to suffer from unreasonable, dangerous side effects.

62. Lilly was negligent in the design, manufacture, testing, advertising, marketing, promoting, labeling, supply, and sale of Cymbalta in that it:

a. Failed to provide proper warnings that fully and accurately inform users and health care professionals about the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms;

b. Failed to provide warnings that Cymbalta could cause users to become physically dependent on the drug;

c. Failed to provide adequate training and instructions to users and health care professionals regarding appropriate methods for stopping Cymbalta, including the results of clinical trials showing that there was no differences observed between abrupt or tapered discontinuation;

d. Misled users by suggesting that Cymbalta withdrawal was rare;

e. Failed to warn that the risks associated with Cymbalta exceeded the risks of other comparable forms of treatment options;

f. Failed to warn of the potential duration of withdrawal symptoms associated with Cymbalta;

g. Misrepresented the severity of symptoms associated with withdrawal;

h. Negligently designed Cymbalta in a way that it knew would cause withdrawal and physical dependency;

i. Negligently marketed Cymbalta despite the fact that the risk of withdrawal symptoms was so high and the benefits of the drug were so questionable that no reasonable pharmaceutical company, exercising due care, would have placed it on the market;

j. Recklessly, falsely, and deceptively represented or knowingly omitted, suppressed, or concealed, material facts regarding the safety of Cymbalta to Plaintiff Lisa D. Carpenter, the public, and the medical community;

k. Failed to comply with its post-manufacturing duty to warn that Cymbalta was being promoted, distributed, and prescribed without adequate warnings that fully and accurately inform users and physicians of the true frequency, severity, and/or duration of potential withdrawal symptoms; and

l. Was otherwise careless, negligent, grossly negligent, reckless, and acted with willful and wanton disregard for Plaintiff Lisa D. Carpenter's rights and safety.

63. Despite the fact that Lilly knew, or should have known, that Cymbalta caused frequent and severe withdrawal symptoms, Lilly continued to market Cymbalta to consumers, including Plaintiff Lisa D. Carpenter, without adequate instructions for stopping Cymbalta and without adequate warnings about the frequency, severity, and/or duration of the withdrawal symptoms. Lilly knew, or should have known, that Cymbalta users would suffer foreseeable injuries as a result of its failure to exercise ordinary care, as described above. Lilly knew or should have known that Cymbalta was defective in design or formulation in that, when it left the

hands of the manufacturer and/or suppliers, the foreseeable risks exceeded the benefits associated with the design or formulation.

64. Had Lilly provided adequate instructions for the proper method for stopping Cymbalta and/or adequate warnings regarding the frequency, severity, and/or duration of its withdrawal symptoms, Plaintiff Lisa D. Carpenter's injuries would have been avoided.

65. As a direct and proximate result of one or more of these wrongful acts and omissions of Lilly, Plaintiff Lisa D. Carpenter suffered significant injuries as set forth herein. Plaintiff Lisa D. Carpenter has incurred and will continue to incur physical and psychological pain and suffering, emotional distress, sorrow, anguish, stress, shock, and mental suffering. Plaintiff Lisa D. Carpenter has required and will continue to require healthcare and services and has incurred, and will continue to incur medical and related expenses. Plaintiff Lisa D. Carpenter has also suffered and will continue to suffer diminished capacity for the enjoyment of life, a diminished quality of life, aggravation of preexisting conditions and activation of latent conditions, and other losses and damages.

66. WHEREFORE, Plaintiffs demand judgment against Lilly for compensatory, statutory and punitive damages, together with interest, costs of suit, and all such other relief as the Court deems appropriate pursuant to the common law and statutory law.

SECOND CAUSE OF ACTION
STRICT PRODUCT LIABILITY – DESIGN DEFECT

67. Plaintiffs incorporate by reference, as if fully set forth herein, all other paragraphs of this First Amended Complaint.

68. Lilly is, and was at all times relevant herein, engaged in the business of designing, testing, manufacturing, and promoting prescription medications, including Cymbalta, to citizens of the State of New Hampshire, including Plaintiff Lisa D. Carpenter.

69. Lilly manufactured, marketed, promoted, and sold a product that was merchantable and/or reasonably suited to the use intended. Cymbalta was expected to, and did, reach Plaintiff Lisa D. Carpenter without substantial change in the condition in which it was sold. Its condition when sold was the proximate cause of the injuries sustained by Plaintiff Lisa D. Carpenter.

70. Lilly introduced a product into the stream of commerce that is defective in design, in that the foreseeable risks of harm posed by the product could have been reduced or avoided by the adoption of a reasonable alternative design by Lilly, and Lilly's omission of the alternative design renders the product not reasonably safe. The harm of Cymbalta's design outweighs any benefit derived therefrom. The unreasonably dangerous nature of Cymbalta caused serious harm to Plaintiff Lisa D. Carpenter. Lilly placed Cymbalta into the stream of commerce with wanton and reckless disregard for public safety.

71. Lilly knew or should have known that physicians and other health care providers began commonly prescribing Cymbalta as a safe product despite the fact that the design of Cymbalta pills, as delayed-release capsules of beads at 20, 30 and 60 mg doses only, along with the instruction to swallow them whole, prevents users from being able to properly taper (gradual decrease in dosage) from Cymbalta in order to avoid or reduce withdrawal symptoms. Cymbalta users such as Plaintiff are thus unable to avoid the danger of Lilly's design upon cessation of treatment. Moreover, Lilly knew that the likelihood of experiencing withdrawal symptoms (such that gradual tapering would be required) is significant. Lilly was aware of this problem before Cymbalta was approved by the FDA and took no action to obtain approval of Cymbalta in a different design, which would have eliminated the risks associated with Cymbalta's defect.

72. Lilly could have redesigned Cymbalta at a reasonable cost in order to allow users to taper gradually and thus with less risk of injury, and could have made such different designs

before Cymbalta was approved by the FDA in 2004. The risk of harm inherent in Lilly's design of Cymbalta capsules outweighs the utility of its design. There are other antidepressant medications and similar drugs on the market with safer alternative designs with respect to patients' and physicians' ability to gradually decrease the dosage. These other antidepressant medications existed in the market prior to Lilly seeking FDA approval for Cymbalta, including Lilly's other blockbuster antidepressant, Prozac.

73. As a direct and proximate result of Lilly's widespread promotional activities, physicians commonly prescribe Cymbalta as safe.

74. Lilly took no action either prior to FDA approval or post-approval to include a warning in the Cymbalta labeling warning patients and doctors about Cymbalta's design defect.

75. As a direct and proximate result of one or more of these wrongful acts and omissions of Lilly, Plaintiff Lisa D. Carpenter suffered significant injuries as set forth herein. Plaintiff Lisa D. Carpenter has incurred and will continue to incur physical and psychological pain and suffering, emotional distress, sorrow, anguish, stress, shock, and mental suffering. Plaintiff Lisa D. Carpenter has required and will continue to require healthcare and services and has incurred, and will continue to incur medical and related expenses. Plaintiff Lisa D. Carpenter has also suffered and will continue to suffer diminished capacity for the enjoyment of life, a diminished quality of life, aggravation of preexisting conditions and activation of latent conditions, and other losses and damages.

76. WHEREFORE, Plaintiffs demand judgment against Lilly for compensatory, statutory and punitive damages, together with interest, costs of suit, and all such other relief as the Court deems appropriate pursuant to the common law and statutory law.

THIRD CAUSE OF ACTION
STRICT PRODUCT LIABILITY – FAILURE TO WARN

77. Plaintiffs incorporate by reference, as if fully set forth herein, all other paragraphs of this First Amended Complaint.

78. Lilly researched, tested, developed, designed, licensed, manufactured, packaged, inspected, labeled, distributed, sold, marketed, promoted and/or introduced Cymbalta into the stream of commerce and in the course of same, directly advertised and/or marketed Cymbalta to consumers or persons responsible for consumers, and therefore, had a duty to warn Plaintiff Lisa D. Carpenter and Plaintiff Lisa D. Carpenter's physicians of the risks associated with stopping Cymbalta, which Lilly knew or should have known are inherent in the use of Cymbalta.

79. Lilly had a duty to warn users and physicians fully and accurately of the frequency, severity, and/or duration of Cymbalta's withdrawal symptoms which it knew or should have known, can be caused by the discontinuation of Cymbalta and/or are associated with Cymbalta discontinuation, including nausea, twitching, insomnia, Restless Leg Syndrome, throbbing pain in legs and arms, headaches, eye aches, excessive sweating, chills, tiredness and flu-like symptoms. Furthermore, Lilly had a duty to provide users and physicians with adequate instructions for stopping Cymbalta.

80. Cymbalta was under the exclusive control of Lilly and was neither accompanied by adequate instructions for stopping Cymbalta nor accompanied by adequate warnings regarding the frequency, severity, and/or duration of symptoms associated with the discontinuation of Cymbalta. The information given to consumers and physicians did not properly instruct users and physicians on how to stop Cymbalta and did not accurately reflect the risk, incidence, symptoms, scope, or severity of the withdrawal symptoms as compared to other similar products available in the market, which possessed lower risk of such symptoms. The

promotional activities of Lilly further diluted and/or minimized any warnings that were provided with the product.

81. Lilly misled users and health care professionals as to the severity, frequency, and/or duration of Cymbalta withdrawal symptoms in order to foster and heighten sales of the product.

82. Following Cymbalta's approval by the FDA in 2004, Lilly conducted additional clinical trials, studies, and re-analyses about Cymbalta withdrawal and could have used data obtained in those studies and results to make changes to the Cymbalta label pursuant to the Changes Being Effected regulation.

83. Cymbalta was defective and unreasonably dangerous when it left the possession of Lilly in that it contained instructions insufficient to fully inform users and physicians on how to stop Cymbalta and that it contained warnings insufficient to alert Plaintiff Lisa D. Carpenter to the dangerous risks and reactions associated with it, including but not limited to severe, debilitating withdrawal symptoms. Even though Lilly knew or should have known the risks associated with Cymbalta, it failed to provide adequate instructions and warnings.

84. The foreseeable risks of withdrawal-related harm posed by Cymbalta could have been reduced or avoided by the provision of reasonable instructions or warnings by Lilly. Lilly's omission of reasonable instructions or warnings rendered Cymbalta not reasonably safe.

85. Plaintiff Lisa D. Carpenter used Cymbalta as intended or in a reasonably foreseeable manner.

86. Plaintiff Lisa D. Carpenter could not have discovered any defect in the drug through the exercise of reasonable care.

87. Lilly, as manufacturer of Cymbalta and other pharmaceutical prescription drugs, is held to the level of knowledge of an expert in the field, and further, Lilly had knowledge of the

dangerous risks associated with the discontinuation of Cymbalta.

88. Plaintiff Lisa D. Carpenter did not have the same knowledge as Lilly and no adequate warning was communicated to her physicians.

89. Lilly had a continuing duty to warn users, including Plaintiff Lisa D. Carpenter and her physicians, and the medical community of the dangers associated with Cymbalta discontinuation. By negligently and wantonly failing to provide adequate instructions and failing to adequately warn of the withdrawal symptoms associated with Cymbalta discontinuation, Lilly breached its duty.

90. Although Lilly knew or should have known of Cymbalta's withdrawal symptoms, it continued to design, manufacture, market, and sell the drug without providing adequate warnings or instructions concerning the use of the drug in order to maximize sales and profits at the expense of the public health and safety, in knowing, conscious, and deliberate disregard of the foreseeable harms posed by the drug.

91. In addition, Lilly's conduct in the packaging, warning, marketing, advertising, promoting, distribution, and sale of the drug was committed with knowing, conscious, willful, wanton, and deliberate disregard for the value of human life, and the rights and safety of consumers, including Plaintiff Lisa D. Carpenter.

92. As a direct and proximate result of one or more of these wrongful acts and omissions of Lilly, Plaintiff Lisa D. Carpenter suffered severe injuries as set forth herein. Plaintiff Lisa D. Carpenter has incurred and will continue to incur physical and psychological pain and suffering, emotional distress, sorrow, anguish, stress, shock, and mental suffering. Plaintiff Lisa D. Carpenter has required and will continue to require healthcare and services and has incurred, and will continue to incur medical and related expenses. Plaintiff Lisa D. Carpenter has also suffered and will continue to suffer diminished capacity for the enjoyment of life, a

diminished quality of life, aggravation of preexisting conditions and activation of latent conditions, and other losses and damages.

93. WHEREFORE, Plaintiffs demands judgment against Lilly for compensatory, statutory and punitive damages, together with interest, costs of suit, and all such other relief as the Court deems appropriate pursuant to the common law and statutory law.

FOURTH CAUSE OF ACTION
NEGLIGENT MISREPRESENTATION

94. Plaintiffs incorporate by reference, as if fully set forth herein, all other paragraphs of this First Amended Complaint.

95. Lilly owed a duty to Plaintiff Lisa D. Carpenter and her physicians to convey and communicate truthful and accurate information about Cymbalta.

96. Lilly represented to Plaintiff Lisa D. Carpenter, her physicians, and other members of the public and the medical community that Cymbalta was safe for use and that any withdrawal symptoms were no different, no worse, and no more frequent, than those of other similar products on the market. These representations were, in fact, false. Lilly's representations on the Cymbalta label suggested that withdrawal was rare, or that withdrawal symptoms occurred at a rate of approximately 1% or 2%, without mentioning the overall percentage of users who will experience withdrawal symptoms, which Lilly's own studies showed to be, at minimum, 44%.

97. Lilly was negligent in failing to exercise due care in making the aforesaid representations.

98. Lilly had a pecuniary interest in making said representations, which were made in order to expand sales and increase revenue from Cymbalta.

99. At the time said representations were made by Lilly, at the time Plaintiff Lisa D. Carpenter and her physicians took the actions herein alleged, Plaintiff Lisa D. Carpenter and her

physicians were ignorant of the falsity of Lilly's representations and reasonably believed them to be true. In justifiable reliance upon said representations, Plaintiff Lisa D. Carpenter and her physicians were induced to, and did, use Cymbalta and attempt to discontinue Cymbalta. If Plaintiff Lisa D. Carpenter and her physicians had known the actual facts, Plaintiff Lisa D. Carpenter's injuries would have been avoided because Plaintiff Lisa D. Carpenter's physician either would not have prescribed the drug, Plaintiff Lisa D. Carpenter would not have taken the drug, and/or the risk would have been conveyed to Plaintiff Lisa D. Carpenter in a way so as to alter the prescription and avoid Plaintiff Lisa D. Carpenter's injuries.

100. The reliance of Plaintiff Lisa D. Carpenter and her physicians upon Lilly's representations was justified because the representations were made by individuals and entities who appeared to be in a position to know the true facts relating to risks associated with Cymbalta.

101. As a direct and proximate result of one or more of these wrongful acts and omissions of Lilly, Plaintiff Lisa D. Carpenter suffered pecuniary losses including but not limited to past and future medical and related expenses.

102. WHEREFORE, Plaintiffs demand judgment against Lilly for compensatory, statutory and punitive damages, together with interest, costs of suit, and all such other relief as the Court deems appropriate pursuant to the common law and statutory law.

FIFTH CAUSE OF ACTION
FRAUD

103. Plaintiffs incorporate by reference, as if fully set forth herein, all other paragraphs of this First Amended Complaint.

104. As the United States Supreme Court stated in *Wyeth v. Levine*, "…it has remained a central premise of federal drug regulation that the manufacturer [of a prescription drug, such as Cymbalta] bears responsibility for the content of its label at all times. It is charged both with

crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." 555 U.S. 555, 571 (2009).

105. Lilly committed fraud by actively concealing material adverse information that was in its possession from its labeling and marketing of Cymbalta, including but not limited to, concealing the true frequency, severity and duration of Cymbalta's withdrawal side effects and falsely represented the withdrawal risk associated with Cymbalta.

106. Lilly, through its clinical trial data, knew that, when it made the misrepresentations and/or omissions set forth herein, they were false, that patients and medical professionals would rely upon its misrepresentations and omissions, and that the misrepresentations were intended to cause patients like Plaintiff to purchase and ingest Cymbalta.

107. The specific acts of Lilly include, *inter alia*, the following:

a. Fraudulently suggesting that the withdrawal risk is rare, or occurred at a rate of approximately one (1) percent, when the overall rate of patients experiencing withdrawal, according to Lilly's own clinical trials, is high (between 44.3% to 78%, depending on whether Lilly systematically measured the risk). Furthermore, an analysis of the data from Lilly's clinical trials reveals, with statistically significant results, that in comparison to stopping a placebo, stopping Cymbalta elevated the risk of specific withdrawal symptoms as much as 23-fold (i.e., nausea 23-fold, dizziness 17-fold, paresthesia 11-fold, irritability 9-fold, nightmares 8-fold, headaches 7-fold, and vomiting 4-fold);

b. Fraudulently omitting material information in its labeling and marketing concerning the severity of Cymbalta withdrawal including the fact that, in some of Lilly's clinical trials, between 9.6% and 17.2% suffered severe withdrawal (approximately 50% suffered moderate withdrawal);

c. Fraudulently omitting material information in its labeling and marketing concerning the duration of Cymbalta withdrawal. In fact, more than 50% of patients in the Cymbalta clinical trials continued to suffer from withdrawal symptoms two weeks after coming off the drug. Lilly deliberately did not monitor withdrawal beyond two weeks in any of its clinical trials, because Lilly did not want to obtain any adverse data that it would be obliged to disclose to patients and doctors. Lilly did this notwithstanding the fact that Lilly was well aware that withdrawal symptoms could be protracted. For instance, the Cymbalta Summary of Product Characteristics" (SmPC) in Europe stated that, "in some

individuals [withdrawal symptoms] may be prolonged (2-3 months or more)." The Practice Guideline for the Treatment of Patients With Major Depressive Disorder, Third Edition, published in 2010 (in which at least three Lilly consultants were on the working group and review panel) states under "Discontinuation syndrome" that "some patients do experience **more protracted** discontinuation syndromes, particularly those treated with paroxetine [Paxil]" and "as with SSRIs, abrupt discontinuation of SNRIs should be avoided whenever possible. Discontinuation symptoms, **which are sometimes protracted**, are more likely to occur with venlafaxine [Effexor] (and, by implication devenlafaxine [Pristiq]) than duloxetine [Cymbalta] (100) and may necessitate a slower downward titration regimen or change to fluoxetine." In truth, however, Lilly's own clinical studies, completed after the FDA approved Cymbalta, show that Cymbalta and Effexor are equally as bad as each other when it comes to withdrawal;

d. Purposefully failing to use systematic monitoring with a withdrawal symptom checklist in the Cymbalta studies underlying Perahia's analysis, whereas in earlier Lilly-sponsored studies comparing Prozac to Paxil, Zoloft, and Effexor, Lilly systematically monitored withdrawal using a symptom checklist. Lilly was well aware of the withdrawal risk because it had orchestrated a marketing campaign differentiating Prozac from competitor antidepressants based on Prozac's comparatively long half-life. In fact, based on Cymbalta's half-life (the second shortest half-life between Effexor and Paxil), one would expect the true risk of withdrawal to be in a range between 66% and 78%. *See* Glenmullen, The Antidepressant Solution – A Step-by-Step Guide to Safely Overcoming Antidepressant Withdrawal, Dependence, and "Addiction" (2005). Internal documents show that Lilly's decision to avoid using the checklist was deliberate, so as to avoid obtaining adverse data that would end up in the labeling;

e. Because Cymbalta's half-life is the second shortest and the closest to Effexor's, Lilly must have recognized that the risk of Cymbalta withdrawal was substantial, as confirmed by its own clinical trial data, and likely much worse as explained above. However, rather than being forthcoming about this important risk, Lilly instead chose to obscure the risk by using misleading language in its labeling and marketing;

f. Lilly obscured Cymbalta's true withdrawal risks by deflecting attention away from the Cymbalta-specific clinical trial data showing a clear and significant risk and focusing instead on other SSRIs and SNRIs. For instance, Lilly's label stated "During marketing of other SSRIs and SNRIs … there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt …" Lilly's use of "spontaneous" reports from "other SSRIs or SNRIs" is misleading given that approximately 40% to 50% of patients in Lilly's own clinical trials of Cymbalta reported adverse events. In using this language, Lilly misleadingly suggests that the withdrawal risks associated with other SSRIs and SNRIs are worse than Cymbalta's risks, which is the opposite of the truth – Cymbalta is one of the worst as confirmed in Lilly's own clinical data;

g. In addition to failing to warn about these known risks, Lilly utilized paid Key Opinion Leaders ("KOLs") to endorse the safety and efficacy of Cymbalta and assure prescribing doctors that Cymbalta's withdrawal risks were not as frequent, severe or protracted as they really are. In the material used by these KOLs to promote Cymbalta to other physicians, Lilly deliberately avoided disclosing the data it possessed about discontinuation, even though KOLs were requesting them. Moreover, Lilly never trained its KOLs to be able to make evidenced-based recommendations about tapering or down-titration, despite Lilly's awareness that this issue was important to prescribers. In one internal email, dated December 5, 2005, Lilly personnel discussed the concerns raised by a prominent KOL used by Lilly. In the email, the doctor stated that his observations of withdrawal were more common than Lilly was disclosing and specifically requested a presentation about Lilly's data surrounding withdrawal. Despite this request, Lilly never gave a presentation to KOLs educating these promoters about Cymbalta's withdrawal risks;

h. Similarly, the American Psychiatric Publishing Textbook of Psychiatry, Fifth Edition with a Foreword written by the same Lilly consultant and KOL, Dr. Schatzberg, published in 2008, makes no mention of Cymbalta nor the frequency, severity or duration of Cymbalta withdrawal. Indeed, the text states:

> Discontinuation symptoms appear to occur most commonly after discontinuation of short-half-life serotonergic drugs (Coupland et al. 1996), such as fluvoxamine [Luvox], paroxetine [Paxil], and venlafaxine [Effexor]. There is no mention of Cymbalta although it had been on the market for four years and has a shorter-half than either Luvox or Paxil. Indeed, it had the second shortest half-life next to Effexor;

i. Lilly also appears to have engaged in selective and biased publication of its clinical trials of Cymbalta. In a recent study published in the New England Journal of Medicine, researchers obtained clinical trials for antidepressants (including Cymbalta) that had been submitted to the FDA and compared them with studies that had been published. The authors found that there was a "bias towards the publication of positive results" and that, "according to the published literature, it appeared that 94% of the trials conducted were positive. By contrast, the FDA analysis shows that 51% were positive." The authors found that, as a result of such selective publication, the published literature conveyed a misleading impression of Cymbalta's efficacy resulting in an apparent effect-size that was 33% larger than the effect size derived from the full clinical trial data. *See* Erick H. Turner et al., Selective Publicationof Antidepressant Trials and Its Influence on Apparent Efficacy, 358 NEW ENG. J. MED. 252 (2008).

108. When the above representations and/or omissions were made by Lilly, it knew those representations and/or omissions to be false, or willfully and wantonly and recklessly disregarded whether the representations and/or omissions were true. These representations

and/or omissions were made by Lilly with the intent of defrauding and deceiving the public and the prescribing medical community and with the intent of inducing the public to take Cymbalta and the medical community (including Plaintiff's doctor) to recommend, prescribe, and dispense Cymbalta to their patients without adequate warning.

109. At the time the aforementioned representations or omissions were made by Lilly, and at the time Plaintiff purchased and began to ingest Cymbalta, Plaintiff was unaware of the falsity of Lilly's representations and/or omissions and reasonably relied upon Lilly's representations and omissions.

110. In reliance upon Lilly's representations and/or omissions, Plaintiff was induced to take Cymbalta and suffered significant withdrawal side effects.

111. Lilly's motive in failing to advise physicians and the public of Cymbalta's withdrawal risks was financial gain along with its fear that, if accompanied by proper and adequate information, Cymbalta would lose its share of the antidepressant market.

112. At all times herein mentioned, the actions of Lilly, its agents, servants, and/or employees were wanton, grossly negligent, and reckless and demonstrated a complete disregard and reckless indifference to the safety and welfare of Plaintiff in particular and to the general public in that Lilly did willfully and knowingly place the dangerous and defective drug Cymbalta on the market with the specific knowledge that it would be sold to, prescribed for, and used by members of the public and without adequate instructions for use.

113. Punitive damages would be particularly appropriate for Lilly in this case given that fraud and concealment appear to be a part of its modus operandi. Since the 1980s, Lilly has had an ongoing history of concealing serious side effects associated with its drugs and illegally promoting its drugs. For example, in 1985, Lilly and one of its officers pled guilty to multiple criminal counts of violating the Food Drug and Cosmetic Act ("FDCA") arising out of Lilly's

concealment of serious liver and kidney dysfunctions associated with its arthritis drug Oraflex. In 2009, Lilly agreed to plead guilty and pay $1.415 billion to the federal government for illegally promoting Zyprexa. This resolution included a criminal fine of $515 million, which, at the time, was the largest settlement ever in a health care case, and the largest criminal fine for an individual corporation ever imposed in a United States criminal prosecution of any kind.

114. At *all time*s relevant herein, Lilly's conduct was malicious, fraudulent, and oppressive toward Plaintiff in particular and the public generally, and Lilly conducted itself in a willful, wanton, and reckless manner. Despite Lilly's specific knowledge regarding Cymbalta's withdrawal risks as set forth above, Lilly deliberately recommended, manufactured, produced, marketed, sold, distributed, merchandised, labeled, promoted, and advertised Cymbalta as being safe, with minimal withdrawal risks.

115. All of the foregoing constitutes an utter, wanton, and conscious disregard of the rights and safety of a large segment of the public. Thus, Lilly is guilty of reckless, willful, and wanton acts and omissions which evidence a total and conscious disregard for the safety of Plaintiff and others which proximately caused the injuries described herein. Therefore, Plaintiff requests punitive and exemplary damages in an amount to be determined at trial to deter Lilly from continuing its conscious disregard of the rights and safety of the public at large and to set an example so Lilly – as well as other similarly situated drug manufacturers – will refrain from acting in a manner that is wanton, malicious, and in utter, conscious disregard of the rights of a large segment of the public.

116. As a direct and proximate result of Lilly's false representations and/or omissions, Plaintiff has suffered serious injury, incurred and will in the future incur expenses, lost income and sustained other damages, including but not limited to pain and suffering, emotional distress, sorrow, anguish, stress, shock and mental suffering.

SIXTH CAUSE OF ACTION
BREACH OF IMPLIEDWARRANTY

117. Plaintiffs incorporate by reference, as if fully set forth herein, all other paragraphs of this First Amended Complaint.

118. Lilly made numerous representations, descriptions, and promises to Plaintiff Lisa D. Carpenter regarding the frequency, severity and/or duration of withdrawal symptoms caused by ceasing to take Cymbalta. Accordingly, Lilly expressly warranted that Cymbalta had a low or rare incidence of withdrawal symptoms.

119. As described herein, Plaintiff Lisa D. Carpenter suffered injuries as a direct and proximate result of her discontinuation of Cymbalta.

120. At the time of Plaintiff Lisa D. Carpenter's use of Cymbalta and resulting injuries, the Cymbalta she was taking was in essentially the same condition as when it left the control and possession of Lilly.

121. At all times relevant, the Cymbalta received and used by Plaintiff Lisa D. Carpenter was not fit for the ordinary purposes for which it is intended to be used in that, *inter alia*, it posed a higher risk of withdrawal symptoms – of greater duration and severity – than other similar products available in the market.

122. Plaintiff Lisa D. Carpenter's injuries were due to the fact that Cymbalta was in a defective condition, as described herein, rendering it unreasonably dangerous to her.

123. As a direct and proximate result of one or more of these wrongful acts and omissions of Lilly, Plaintiff Lisa D. Carpenter suffered significant injuries as set forth herein. Plaintiff Lisa D. Carpenter has incurred and will continue to incur physical and psychological pain and suffering, emotional distress, sorrow, anguish, stress, shock, and mental suffering. Plaintiff Lisa D. Carpenter has required and will continue to require healthcare and services and has incurred, and will continue to incur medical and related expenses. Plaintiff Lisa D. Carpenter

has also suffered and will continue to suffer diminished capacity for the enjoyment of life, a diminished quality of life, aggravation of preexisting conditions and activation of latent conditions, and other losses and damages.

124. WHEREFORE, Plaintiffs demand judgment against Lilly for compensatory, statutory and punitive damages, together with interest, costs of suit, and all such other relief as the Court deems appropriate pursuant to the common law and statutory law.

SEVENTH CAUSE OFACTION
LOSS OF CONSORTIUM

125. Plaintiffs incorporate all paragraphs of this First Amended Complaint as if set forth herein.

126. At all times herein mentioned, Plaintiffs were, and are, legally married as husband and wife.

127. As a direct and proximate result of Lilly's aforementioned conduct, and as a result of the injuries and damages to Plaintiff Lisa D. Carpenter, her husband, Plaintiff Jeffrey D. Carpenter, has been deprived of the love, companionship, comfort, affection, society, solace or moral support, protection, loss of enjoyment of sexual relations, and loss of physical assistance in the operation and maintenance of the home, and has thereby sustained, and will continue to sustain, damages.

128. WHEREFORE, Plaintiffs demand judgment against Defendant and seek compensatory damages, and exemplary and punitive damages together with interest, the costs of suit and attorneys' fees and such other and further relief as this Court deems just and proper.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully pray for judgment against Lilly as follows:

a. Judgment in favor of Plaintiffs and against Lilly, for all damages in such amounts as may be proven at trial;

b. Compensation for economic and non-economic losses, including but not limited to, past and future medical expenses, medical monitoring, out-of-pocket expenses, past and future physical pain and mental anguish, past and future physical impairment, past and future loss of companionship and consortium, and past and future loss of household services, in such amounts as may be proven at trial;

c. Past and future general damages, according to proof;

d. Any future damages resulting from permanent injuries;

e. Psychological trauma, including but not limited to mental anguish, mental distress, apprehension, anxiety, emotional injury, psychological injury, depression, and aggravation of any pre-existing and/or underlying emotional or mental diseases or conditions;

f. Pain and suffering;

g. Loss of enjoyment of life;

h. Punitive and exemplary damages in an amount to be determined by trial;

i. Attorneys' fees and costs;

j. Treble damages;

k. Prejudgment and post-judgment interest;

l. Costs to bring this action; and

m. Any such other and further relief as the Court may deem just and proper in law or in equity.

DEMANDS FOR JURY TRIAL

Plaintiffs respectfully request a jury trial of all issues presented in this Complaint.

Dated: June 30, 2015

Respectfully submitted,

BAUM HEDLUND ARISTEI & GOLDMAN, P.C.

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Attorneys for Plaintiffs

CERTIFICATE OF SERVICE

I, R. Brent Wisner, hereby certify that, on June 30, 2015, I electronically filed Plaintiffs' **FIRST AMENDED COMPLAINT** with the Clerk for the United States District Court for the District of New Hampshire using the CM/ECF system, which shall send electronic notification to counsel of record.

/s/ R. Brent Wisner
R. Brent Wisner